Phase I/II Study of GM-CSF Gene-modified Autologous Tumor Vaccines in Early and Advanced Stage Non-Small Cell Lung Cancer (NSCLC)

Non-Technical Abstract

No consistently effective therapy exists for metastatic Non-Small Cell Lung Carcinoma (NSCLC); therefore, a significant unmet medical need for a more effective therapy still exists for NSCLC. The preliminary results from a trial at the Dana Farber Cancer Institute, which is identical to the proposed study (See RAC Protocol 9707-203), are encouraging and warrant further investigation and validation of these results in additional subjects with NSCLC.

The rationale for cancer vaccine therapy is to modify relatively non-immunogenic tumors to induce a tumor-specific immune response in the patient. Cancer cell vaccines, genetically modified to secrete cytokines, have generated potent anti-tumor immunity in preclinical animal models of melanoma, lymphoma, colon, renal, lung, and prostate cancer. Secretion of GM-CSF by genetically modified tumor cells stimulates cytokine release at the vaccine site to activate antigen presenting cells, which prime $CD4^+$ and $CD8^+$ T cells to recognize circulating tumor-associated antigens, thereby inducing a tumor specific cellular immune response. Induction of a tumor specific humoral immune response and activation of a granulocytic (e.g. eosinophils and neutrophils) inflammatory reaction may also contribute to the efficacy of this approach.

The proposed study is a phase I/II open-label, outpatient clinical trial using Autologous NSCLC GVAX® Vaccine in 60 subjects with both early and advanced NSCLC. This will allow us to compare the vaccine induced anti-tumor immune response between these two patient groups. Vaccinations with Autologous NSCLC GVAX® Vaccine will be administered on a biweekly schedule for a total of 6 vaccinations and subjects will be followed for 12 months from initiation of study treatment. The vaccine dose will be individualized for each patient based on the total vaccine yield and will range from 5×10^6 to 5×10^7 cells/dose. This will enable each patient to receive the maximum possible dose and will allow for a uniform schedule of 6 vaccinations per patient. The minimum dose of 5×10^6 cells/vaccine was selected as previous trials of autologous GM-CSF modified tumor vaccines in melanoma, renal cell carcinoma, and NSCLC have suggested that this is the minimum effective dose for induction of reliable anti-tumor immune responses as measured by delayed-type hypersensitivity (DTH) reactivity. We do not anticipate any serious or unexpected vaccine related toxicities at the dose levels planned in this trial based on the lack of significant toxicity noted in previous trials of autologous and allogeneic GVAX® that have utilized individual doses up to 5×10^8 cells. The primary objectives of this trial include analysis of vaccine safety, measurement of anti-tumor immune response, comparison of immune response between early and advanced stage patients, and measurement of radiologic tumor response, assessment of the feasibility and consistency of vaccine manufacturing,. Secondary objectives include evaluation of disease free and overall survival.